Exhibit A
Part 2

B. Ethicon knew that the old construction mesh (Prolene) was not appropriate for use in its TVT device as early as 1998, but failed to modify/change the mesh to a larger pore, lighter weight mesh that would not deform, fray, lose particles, rope, curl, degrade, cause excessive foreign body reactions, and cause excessive shrinkage/contraction because of its economic interest in maintaining its competitive advantage in the MUS market and, therefore, Ethicon put profits before patient safety.

As stated above, Ethicon knew from the time it launched the TVT with the mechanically cut mesh that it was defective in multiple respects. This is true because the TVT Prolene mesh was known to be made from heavyweight 6 mil fiber and a construction that allowed for mesh curling, roping, fraying, zipping, particle loss, and sharp edges. In fact, beginning in 1998, Ethicon had already established a "mesh improvement project" in order to improve the mesh. Despite the fact that the project yielded an improved mesh, Ethicon never incorporated those improvements into the TVT.

As early as May of 1997, Ethicon knew that the Prolene mesh was not ideal for use in vaginal tissues.[130] In fact, Ethicon knew of a case at that time were a patient had been treated with Prolene mesh, which protruded through the vagina, requiring excision of the mesh. Ethicon knew that the ideal mesh for use in the vagina should not have any fraying or spiky edges, needed to have large enough pores to encourage in-growth, and should have a low mass density to minimize foreign body reaction.[131] Ethicon then embarked on a project to improve the Prolene mesh used in the TVT product and Ethicon's hernia products. Among the characteristics they sought to improve were the product curling, zipping and unraveling of the mesh after cutting, and crumbling of the mesh.[132] Ethicon noted that if the Prolene mesh was pulled in one direction, the mesh would curl up into a tube, and the mesh would remain in a rolled condition even after the force of the pulling was no longer on the mesh.

[130] ETH.MESH.12006257
[131] ETH.MESH.12006257
[132] ETH.MESH.09264945

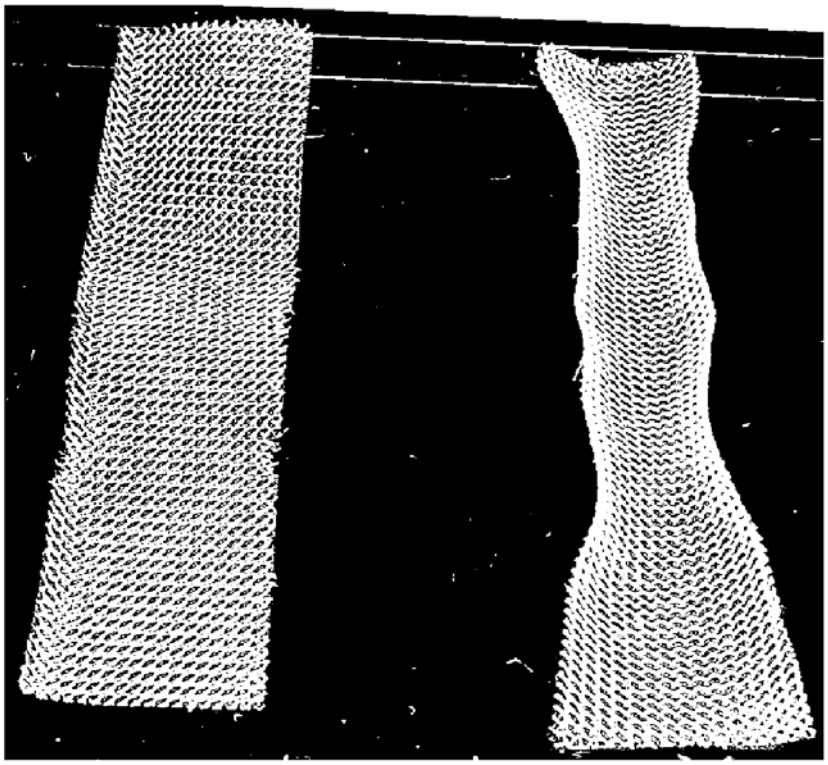


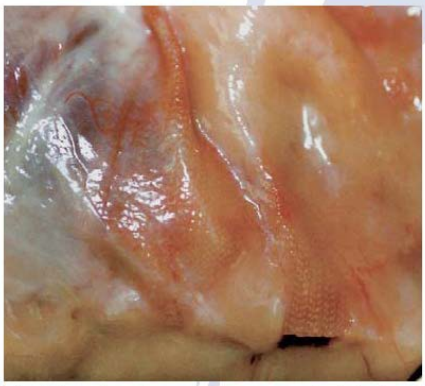
Figure 1 – Control mesh sample before and after the application of the force. A clear picture of mesh curling results.

Ethicon also referred to the original construction 6 mil Prolene mesh as a mesh that was known for its "bad" curling quality.[133] Ethicon ultimately changed the flat Prolene mesh used for hernia repair to address these issues, making changes to the construction of the mesh to address the bad curling quality of the mesh, and at the same time, changing to a lighter weight, 5 mil mesh construction.[134] The change in the mesh construction also made the mesh less likely to fray and lose particles.[135] Despite Ethicon's original intent to incorporate the new construction material which was lighter weight and had improved resistance to curling, fraying, and particle loss,[136] Ethicon continued and still continues to use the original, old, old heavyweight 6 mil construction

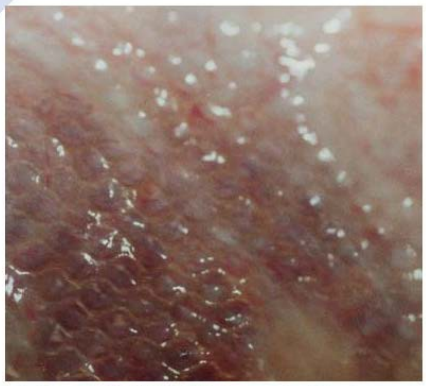
[133] ETH.MESH.02182844, ETH.MESH.00946834.
[134] ETH.MESH.00782152.
[135] ETH.MESH.020008684.
[136] ETH.MESH.09264884.

mesh for the TVT products.[137]

The flaw in the construction of the TVT heavyweight Prolene mesh which allows it to curl into a tube after tensioning or pulling on the mesh and not return to its original shape, combined with the heavyweight and small pore nature of the mesh, causes the mesh to fold up and become hard post-implantation. Ethicon continued to be aware of this continuing defect in the mesh well



Traditional polypropylene mesh. 90 days post-implantation. Fold development (in-vivo study)



Lightweight VYPRO* II mesh. 90 days post-implantation. Fold-free incorporation (in-vivo study)

after the Prolene mesh improvement project was completed and the company changed the construction of its Prolene hernia mesh.[138] Ethicon was also aware that lightweight materials were less likely to fold up post implantation and integrated better with surrounding tissues,[139] but continued to use the heavier 6 mil fibers. The lightweight materials were also much better at resisting crumpling and less likely to have sharp edges during tissue integration.[140]

Ethicon continued to have problems with mesh quality in the TVT mesh after the Prolene mesh improvement project was complete, but never incorporated those changes into the TVT mesh. After the improved construction 5 mil Prolene mesh replaced the 6 mil mesh Prolene mesh for flat hernia repair, Ethicon noted continuing problems with the Prolene mesh

[137] ETH.MESH.09275875, ETH.MESH.02030355.
[138] ETH.MESH.05918776.
[139] ETH.MESH.05446129.
[140] Ethicon Tissue Reinforcement Solutions, 8/21/2004.

in the TVT, noting inconsistent tape width,[141] and fraying and particle loss from the TVT mesh.[142] Doctors reported to Ethicon that the quality of the mesh was terrible, and that particles were falling off the mesh, which was worse when the mesh was elongated.[143]

Even before the TVT was launched in the United States, Ethicon was looking at ways to change the existing mesh tape construction in order to improve the appearance of the mesh and to alleviate problems experienced during the manufacturing process.[144] Ethicon also knew prior to launching the TVT for sale in the United States that if the tape became twisted, it would reduce the effectiveness of the TVT procedure, and evaluated laser-cut samples of the TVT mesh as opposed to the mechanically cut mesh.[145] The project which looked at laser cutting the mesh was part of the "TVT improvement project" which began prior to the launch of the TVT in the United States. Included in the goals of the TVT improvement project were a mesh that was safer, eliminated abrasion, rough edges, and narrowing of the mesh under tension.[146] Ethicon evaluated feedback from surgeons who compared the Laser cut mesh to the guillotine (mechanically) cut mesh, and were told that the laser cut mesh had a more regular appearance, the mesh did not stretch as much as the current guillotine cut mesh, and there was a marked reduction in the amount of loose ends falling off.[147] Testing also showed that the mechanically cut mesh stretched 90% more than the laser cut mesh when force was applied to the mesh. However, despite having a laser cut mesh available which had less rough edges, less particle loss, and less narrowing and deformation under tension, Ethicon chose to launch the TVT in the United States with the guillotine (mechanically) cut mesh.

Ethicon did not change the Prolene mesh in its TVT device despite having better and

[141] ETH.MESH.12002601.
[142] ETH.MESH.00863405.
[143] ETH.MESH.02180833.
[144] ETH.MESH.10591870.
[145] ETH.MESH.12009079.
[146] ETH.MESH.12009262; ETH.MESH.12009276.
[147] ETH.MESH.10182456.

safer options available for economic reasons. Ethicon believed that continued use of the TVT mesh gave the company an economic and competitive advantage in marketing the product because they could continue to use the existing clinical data on the product to market the device, while if the mesh was changed, the existing clinical data would be obsolete.[148] Dr.

Brigitte Hellhammer testified that despite having incorporated the use of the lightweight, large pore Ultrapro mesh in vaginal tissues for the treatment of pelvic organ prolapse, the Ultrapro was never used by Ethicon in a device used for the treatment of stress urinary incontinence largely because the company wanted to continue to rely on the Ulmsten/Nilsson series of studies on 130 patients performed with the TVT device. [149] Dr. Arnaud also confirmed that the company did not want to change anything with the mesh because of the exiting clinical data on the product.[150] It is my opinion to a reasonable degree of medical certainty that Ethicon was negligent in failing to correct the defects in the TVT mesh as the company had knowledge of the defects and failed to correct the defects with products and solutions that were already available to the company because it put its economic interests above the safety of patients.

C. The TVT Laser-Cut Mesh is also innapropriate for use as a permanent implant because it is too stiff and rigid and causes pain and erosions and urinary disfunction as a result

Ethicon started manufacturing and selling the TVT with laser cut mesh in late 2006. The laser cut Prolene mesh in the TVT is cut with a laser in the manufacturing process, as opposed to being mechanically cut.[149] This means that the plastic mesh is cut into strips using a laser instead of a cutting blade.[150] The result is that the mesh itself is stiffer than mechanically cut mesh.[151] In fact, an internal memo from Becky Leibowitz to Paul Parisi and Dan Smith in late 2004 found that

[148] ETH.MESH.03911107.
[149] ETH.MESH.00576844; ETH.MESH.03546997; Smith Dep. (5/15/14) 48:11-17.

[150] Lamont Dep. (9/11/13) 12:13-13:14.
[151] ETH.MESH.01809080-01809081.

when the laser cut mesh was stretched it became about three times stiffer than the machine-cut TVT mesh.[152] Just four years later, it is noted that no clinical study had been done regarding the differences between laser cut mesh and mechanical cut mesh.[153] Nevertheless, Ethicon began regarding its use of the stiffer laser cut mesh.[154] Importantly, while these discussions about the differences between laser cut mesh and mechanical cut mesh were going on, most surgeons using the TVT products did not know what type of mesh they were using.[155] Thus, there was no way for doctors to adjust tensioning differently or be aware that the mesh is stiffer, or to warn patients of an increased risk of erosions and pain. Even as late as February 2015, Ethicon still had not done a single study to determine whether the laser cut mesh causes more erosions than mechanical cut mesh, whether laser cut mesh increases the amount of pain a patient will experience, or any critical outcomes.[156]

The difference in the stretch profile between mechanically cut and laser cut mesh also led Carl G. Nilsson and Christian Falconer, two of the inventors of the original TVT,[157] and Jean de Leval, the inventor of TVT-O, to refuse to use, and question the use, of laser cut mesh.[158] Moreover, according to the J&J Defendants, use of the laser cut mesh would make them unable to rely on the original studies and data they use to tout the safety and effectiveness of the original TVT.[159] Additionally, laser cut mesh was never assessed on its own in a clinical trial.[160]

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[152] ETH.MESH.01809080
[153] ETH.MESH.02090196.

[154] ETH.MESH.00576844.

[155] ETH.MESH.009911296.
[156] Trial Testimony of Katrin Elbert, *Perry v. Luu, et al.*, (2/11/15) 3433:27-3434:18.

[157] Ulmsten U, Falconer C, Johnson P, Jomaa M, Lanner L, Nilsson CG, et al. A multicenter study of tension-free vaginal tape (TVT) for surgical treatment of stress urinary incontinence. Int J Urogynecol J Pelvic Floor Dysfunct 1998;9:210 –3.

[158] ETH.MESH.16416002-16416004; ETH.MESH.04048515-04048520.

[159] ETH.MESH.06040171-06040173.
[160] ETH.MESH.03941617.

Ethicon's Medical Director, Piet Hinoul, even noted in 2011, after the launch of the TVT Exact, that there was is no literature that allows him to discriminate which clinical trials have used laser cut versus mechanical cut.[161]

It is now well known among surgeons and in the published literature that stiff, rigid mesh increases the risk of complications and injuries to women.[162] Based on my experience, training, review of the literature, and review of Ethicon's internal documents, it is my opinion that the laser cut mesh in the TVT is defective because it is too stiff and rigid. As a result, the mesh increases complications including but not limited to chronic pain, chronic dyspareunia, erosions, and urinary dysfunction.

D. Ethicon's TVT's design is flawed because it cannot adequately describe, inform or explain to physicians how to properly "tension" the TVT and the mesh shrinks, contracts, ropes and curls making it impossible to tension.

TVT stands for and has consistently been marketed by Ethicon as "Tension-free Vaginal Tape." Presumably, this means the mesh should be inserted under the urethra without tension. However, the term "tension-free" is misleading. In practice, too little or no tension results in failure to treat the underlying condition of urinary incontinence. On the other hand, as suggested by Ethicon's own internal documents, too much tension can result in serious complications such as retention and urethral erosion.[163] Also, as discussed above, because the mesh shrinks, contracts, ropes and curls, it is impossible or extremely difficult to properly tension the mesh.

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[161] ETH.MESH.00576844. Notably, Dr. Hinoul's trial testimony in *Batiste v. Ethicon*, is in direct contradiction to his statement in this email that all of the TVT-Os tested in his study were laser cut. Presumably in order to convince the doctor to use the laser cut.

[162] Nolfi AL, Brown BN, Liang R, Palcsey SL, Bonidie MJ, Abramowitch SD, Moalli PA, Host Response to Synthetic Mesh in Women with Mesh Complications, *American Journal of Obstetrics and Gynecology* (2016), doi: 10.1016/j.ajog.2016.04.008. Moalli et al, Presentations 8 through 10, Female Pelvic Medicine & Reconstructive Surgery • Volume 17, Number 5, Supplement 2, September/October 2011

[163] ETH.MESH.05529274;ETH.MESH.04044797; ETH.MESH.05529653; ETH.MESH.00161131.

The IFU provides little guidance on proper tensioning of the TVT. Specifically, once the tape is placed, surgeons are simply instructed to pull the needles upwards "to bring the tape (sling) loosely, i.e. without tension, under the midurethra" and to "adjust the tape so that leakage is limited to no more than one or two drops."[164] The IFU's Warnings and Precautions section cautions surgeons to "[e]nsure that the tape is placed with minimal tension under the mid-urethra."[165] Yet in the very same section, the surgeon is instructed "to place the tape tension-free in the mid-urethral position" to minimize the risk of de novo detrusor instability.[166] Finally, the IFU's "Adverse Reactions" section provides that "over correcting, i.e. too much tension applied to the tape, may cause temporary or permanent lower urinary tract obstruction."[167] The IFU's conflicting instructions with regard to tensioning of the tape, "without tension," "with minimal tension," "tension-free" and "overcorrecting, i.e. too much tension" are clearly confusing and inadequate despite the fact that Ethicon knew as early as 2000 that improper tensioning could lead to complications and, therefore, the IFU needed to be "clear."[168] These tension issues are compounded when the mesh contracts, shrinks and deforms as discussed above.

Ethicon recognized as far back as November 1999 that TVT tension adjustment was considered "high need" and surgeons had a hard time sticking to proposed technique.[169] By 2000, Ethicon recognized that excess tensioning during initial placement could create a risk of erosion.[170] In an email dated February 13, 2001, Medical Director Axel Arnaud wrote "there is clearly a need for standardization of the TVT procedure to avoid excessive tension on the mesh. We should aggressively work in order to develop a product and I would like to take the

[164] Eth.Mesh.05222686, emphasis added.
[165] Eth.Mesh.05222687, emphasis added.
[166] Eth.Mesh.05222567, emphasis added.
[167] Eth.Mesh.05222687, emphasis added.
[168] Eth.Mesh.01317523.
[169] Eth.Mesh.05641096.
[170] Eth.Mesh.05529274; Eth.Mesh.04044797; Eth.Mesh.05529653; Eth.Mesh.00161131.

responsibility for this."[171] In May 2002, Axel Arnaud continued to recognize the need to develop a safer device "in order to prevent excess tension of the tape."[172] In 2003, Ethicon recognized that a challenge with the TVT procedure remained complications "associated with over-tensioning of the sling and the inability to obtain precise biofeedback and adjustment during and/or after the procedure."[173] Indeed, Dr. Nilsson, the "father of the TVT", discussed that the TVT done under general anesthesia with a cough test was 70% successful compared to a 85% success rate when done with local anesthesia and a cough test.[174]

The lack of clear direction on tensioning in the IFU is demonstrated in September 2004 emails from Sales Representative Shannon Campbell in which she writes: "What is a huge challenge to a rep trying to make this right, is that we really don't know what the right amount [of tensioning] is. We know this is a quick fix to the problem, but not a clinically backed solution. It's almost like trying to decide if a 8, 10, or 12 mm Hagar dialator is best for tensioning TVT with the patient under general. We learned the cough test, but relied on surgeons experience with the tensioning under general…. This has been such a gray area and everyone seems to have their own tensioning technique." She continues: "I feel I got a little grilled over my suggestion of tensioning, yet there is no clear direction on tensioning. I'm not a rebel looking for my own way of doing this. I'm a rep trying to figure out what is best from my experience with surgeons and what I see the product doing in the OR. …The reason for my question is to see if someone had the proper wording we need to use as rep's that eliminates our liability with the product in the OR concerning tensioning."[175]

In December 2006, Ethicon Marketing Director Allison London-Brown referred to tensioning as a "sticky" question and acknowledged that "we cannot accurately describe

[171] Eth.Mesh.03915380.
[172] Eth.Mesh.03907468.
[173] Eth.Mesh.00259271.
[174] Eth.Mesh.04048515 at Eth.Mesh.0408516 7/01/08 KOL Interview: Carl G. Nilsson, Project Scion.
[175] Eth.Mesh.00864503.

[tensioning] in writing."[176] Meanwhile, Ethicon knew that patients were suffering from erosions and, in fact, would often blame the physician as the cause of the erosion for putting "too much tension on the device."[177] At least by 2007, it seems Ethicon finally acknowledged that "TVT has never been tension free!" despite years of marketing it otherwise.[178] For example, in 1999, Ethicon utilized marketing pieces for "TVT Tension Free Vaginal Tape" which claimed "Tension-free Support Only When Needed" which "reduces possibility of urethral erosion."[179] A 2001 marketing piece for "Gynecare TVT Tension-Free Support for Incontinence" claimed "most complications are minor and are avoidable with adherence to procedural technique and instructions for use."[180] In 2004, during the same time period when Shannon Campbell was lamenting the problems with tensioning, Ethicon continued to promote TVT as "the leader in midurethral sling devices" for 'tension-free support for incontinence."[181] Even after Ethicon acknowledged that TVT has never been tension free, the company continued to market it as "Tension-free Support for Incontinence.[182]

Physicians were also not informed in Ethicon's product IFU that tension on the mesh arms decreases effective pore size and interferes with incorporation into tissue. Engineer Christophe Vailhe testified that "excessive uniaxial tension on the mesh will decrease the pore size and lead to poor tissue integration."[183] In addition, Mr. Vialhe testified that "excessive tension on the mesh would lead to the decrease in pore size that can lead to poor tissue integration . . . ."[184] Engineer Dan Burkley also testified that once the TVT Prolene mesh is either stretched by the surgeon or stretched by in-vivo due to forces in a women's body, it can

[176] Eth.Mesh. 01784428-01784435.
[177] Eth.Mesh.02625055, Eth.Mesh.02627811, Eth.Mesh.02625375, Eth.Mesh.02625155.
[178] Eth.Mesh.06861473.
[179] Eth.Mesh.00161444.
[180] Eth.Mesh.00339437.
[181] Eth.Mesh.00160813.
[182] Eth.Mesh.00164643; Eth.Mesh.00339053.
[183] Vailhe, 6/20/13, 224:10-226:21.
[184] Vailhe, 6/20/13, 224-226.

alter the structure of the pores.[185]

The IFU failed to adequately instruct surgeons on the critical subject of tensioning as repeatedly acknowledged by Ethicon. Ethicon now claims that "tension-free" does not really mean tension-free, but rather, means less tension than as seen in the Burch procedure.[186] Yet, despite its awareness of the problems associated with tensioning, Ethicon failed to revise the conflicting and ambiguous IFU to provide adequate direction on the proper amount of tensioning even though Ethicon was fully aware that improper tensioning could lead to serious complications such as urinary retention, voiding difficulties, de-novo detrusor instability, dyspareunia, vaginal extrusion and urethral erosion. In addition, the design of the device and the mesh is problematic because it shrinks, contracts and deforms exacerbating the issues discussed above.

Ethicon failed to act as a reasonable and prudent medical device manufacturer by failing to design the TVT in a way that it could be properly tensioned and by failing to inform physicians how to properly tension TVT and that improper tension could affect the pore size of the mesh. These failures by Ethicon have resulted in numerous injuries to patients, including, but not limited to chronic pain, urinary retention, voiding difficulties, de-novo detrusor instability, dyspareunia, and vaginal extrusion and urethral erosion.

As one sales representative noted in an email to Dan Smith, the inability of Ethicon to properly communicate how to tension the TVT had safety and legal ramifications:

> I feel I got grilled on my suggestion of tensioning, yet there is no clear direction on tensioning…. My goal is not to get the tape changed, yet strive to place the mesh as designed without altering it. The surgeon does own the responsibility of proper delivery and placement. The fact is, they look to us as reps to show them the proper placement techniques.
> The reason for my question is to see if someone had the proper wording we need to use as reps that eliminates our liability with this product in the OR concerning

[185] Burkley 5/22/13 430:3-431:10.
[186] Smith 6/4/13 524:20-525:13.

tensioning.[187]

In my opinion, Ethicon failed to properly test the unique tensioning issues related to the TVT prior to marketing the device. Ethicon left physicians without sufficient information about how to properly remove sheaths and/or properly tension the TVT mesh in light of the lack of uniformity with tensioning and for failing to account for problems with the mesh like contraction, shrinkage and deformation when tensioning. Ethicon improperly managed the sheath/tension problem by telling individual physicians "tips and tricks" including the Surgeon's Resource Monograph. This advice necessarily could not reach hundreds of surgeons who did not get the "tips and tricks" from sales representatives or Ethicon employees. Such information should have been put in the IFU. Because physicians did not have the proper information, they could not impart the information to their patients or properly consent their patients for all of the risks associated with over-tensioning mesh such as roping, curling, fraying and all of the associated injuries.

E. Ethicon's Prolene mesh in the TVT is not suitable for permanent implant because the Material Safety Data Sheets ("MSDS") for polypropylene resin used to manufacture polypropylene states that polypropylene is incompatible with strong oxidizers such as peroxides which are readily found in the vagina

According to Ethicon Medical Director, Dr. Martin Weisberg, a Material Safety Data Sheet (MSDS) is "a document that discusses the product, the composition, any potential hazards from it . . . Generally, the safety particular of products."[188] As it relates to polypropylene, I have reviewed several MSDSs for polypropylene resin used to manufacturer meshes used in various pelvic floor meshes. All of the MSDSs discussed below are available to the public.

Sunoco, the manufacturer for the polypropylene resin used to manufacture Ethicon's

[187] ETH.MESH.00864503.
[188] Weisberg Dep. (8/9/13) 909:2-9.

pelvic floor products lists the possibility that polypropylene mesh is incompatible with strong oxidizers. This is documented by the Sunoco MSDS[189] from April 13, 2005 which states in relevant part:

> 10. STABILITY AND REACTIVITY
>
> - **INCOMPATIBILITY**
> The following materials are incompatible with this product: Strong oxidizers such as chlorine, peroxides, chromates, nitric acid, perchlorates, concentrated oxygen, sodium hypochlorite, calcium hypochlorite and permanganates. Chlorine; Nitric acid;

This warning is important because it states what the polypropylene in the TVT is incompatible with strong oxidizers like peroxides, which is particularly important because the vagina is a natural and ready source of peroxides. In fact, the vagina is a ready source of hydrogen peroxide production. In a paper titled, "The in vitro effects of hydrogen peroxide on vaginal microbial communities,"[190] the amount of hydrogen peroxide produced by the lactobacillus species is reported. The paper states, “Hydrogen Peroxide reached concentrations of from 0.05 to 1.0 mM, which under intensive aeration increases even up to 1.8 mM." This work confirmed the earlier research in the paper titled, "Hydrogen peroxide produced by Lactobacillus species as a regulatory molecule for vaginal micro-flora.[191] " The human body also contains other agents, such as hydrocarbons and various bacteria that impacts the MSDS discussed above and the warnings contained therein.[192]

The Prolene MSDS indicates that if you put the polypropylene used to make the TVT

[189] ETH.MESH.02026591 at 6591-6595.
[190] M Strus in FEMS Immunol Med Microbiol, 2006 October; 48(1:56-63).
[191] Med Dosw Microbiol. 2004:56(1):67-77.
[192] HB Moon, "Occurrence and accumulation patterns of polycyclic aromatic hydrocarbons and synthetic musk compounds in adipose tissues of Korean females" 2011; "Determination of volatile purgeable halogenated hydrocarbon in human adipose tissue and blood stream," from Bulletin of Environmental Contamination and Toxicology Volume 23 Issue 1 pp 244 – 249 published in 1979; Environmental Health Perspective’s, Vol. 60 pp. 127-131, Henry Anderson, "Utilization of Adipose Tissue Biopsy and Characterizing Human Halogenated Hydrocarbon Exposure", N. Das, Journal Biotechnology Research International 2010, Vol 2011, Article ID 941810 titled, "Review Article: Microbial Degradation of Petroleum Hydrocarbons Contaminant: An Overview”, "Health, Safety and Environment Fact Sheet: Hazardous Substances from CAW/TCA.” (www.caw.ca) August 2011, D. Lithner, 2011, entitled "Environmental and Health Hazards of Chemicals in Plastic Polymers and Products", University of Gothenburg.

mesh in an environment with peroxides, it will start to break down. Given the information available to Ethicon concerning the dangers of polypropylene coupled with the warnings and other contents of the MSDSs and related documents, at a minimum, Ethicon should have conducted clinically relevant testing to determine if naturally occurring conditions in the vagina could cause polypropylene used in the TVT to alter inside a woman's pelvis (as well as other complications). If so, what materials are released into the body as a result, and what impact would those materials have on the body. The fact that the mesh in the TVT is susceptible to breaking down when in contact with peroxides makes it an unsuitable material to be placed in the vagina for the reasons discussed above. At the very least, Ethicon should have disclosed this information to physicians and patients considering use of their pelvic mesh.

Despite the warning in the MSDS for the polypropylene resin used to manufacture the TVT mesh cautioning against contact with strong oxidizers such as peroxides, there is no evidence that Ethicon tested the mesh to see if the peroxides in the vagina broke it down or informed surgeons about this important information contained in this or various other Manufacturer Safety Data Sheets (MSDS) regarding the use of polypropylene.

The fact that the MSDS for the TVT mesh warned against contact with strong oxidizers such as peroxides is information that a doctor would want to consider before implanting a permanent device in a woman's body for the rest of her life as substances in the vagina could cause the breakdown of the product, yet there Ethicon never informed doctors about the warning in the MSDS. As a result, Ethicon failed to act like a reasonable and prudent medical device manufacturer.

F. Ethicon's Prolene mesh is not suitable for permanent implant because the toxicity testing of the polypropylene mesh revealed that it was cytotoxic;

Cytotoxicity means toxicity to the cells causing cell injury or death.[193] In a May 26, 2000, Ethicon Memo titled "Review of biocompatibility on the tension-free vaginal tape (TVT) system for compliance to FDA,"[194] the review contains a "Cytotoxicity Risk Assessment for the TVT (Ulmsten) Device" from August 8, 1997.[195] The Cytotoxicity Assessment states "there is some evidence to suggest that the PP [polypropylene] mesh from the sterile Ulmsten device may have cytotoxic potential.[196] In addition, ISO Elution testing "resulted in marked cytotoxicity in tests conducted at Ethicon (Scotland)."

According to former Ethicon Medical Director, Dr. David Robinson, Ethicon never performed "a single long-term study . . . to determine whether or not the Ethicon mesh is clinically cytotoxic in women."[185] In addition, in its IFUs and Patient Brochures, Ethicon never informed physicians or their patients about the possibility of cytotoxicity.[197] Dr. Robinson testified that if there is a clinical related outcome related to cytotoxicity, it is reasonable for physicians to want to know that the mesh in the TVT product had been tested multiple times to be severely or marked cytotoxic.[198]

Cytotoxicity can cause death to cells that can lead to an inflammatory response leading to a multitude of injuries, including serious adverse complications such as erosions, chronic pelvic pain, recurrence, worsening incontinence, dyspareunia, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction or the need for additional surgeries. Ethicon did not undertake any long term testing to determine whether the marked cytotoxicity found in the TVT mesh had long term consequences for permanent human use.

[193] Robinson Dep. (9/11/13) 1091:11-21.
[194] ETH.MESH.06852118 at 2118-2129 (5/26/2000 Biocompatibility Review).
[195] ETH.MESH.06852120 (8/8/1997 Cytotoxicity Risk Assessment).
[196] *Id.* and Robinson Dep. 9/11/13) 1101:24-1102-5
[197] Robinson Dep. (9/11/13) 1114:15-18.
[198] Robinson Dep. (9/11/13) 1115:5-19.

This is true despite the fact that its own test results showed the mesh to by cytotoxic.

Because of the dangers and consequences that occur as a result of cytotoxicity, the fact that Ethicon had positive tests for cytotoxicity and did nothing to test for it makes the mesh in the TVT not suitable for permanent implantation. In addition, the potential for cytotoxicity or cell death is important information that physicians need to know in order to pass the information on to their patients so that an informed decision can be made about whether to have a permanent medical device implanted in their body. It is clear from Ethicon's Medical Director David Robinson that this information was never passed on to physicians despite the fact that it would have been reasonable for physicians to have this information. As a result, Ethicon did not act as a reasonably prudent medical device manufacturer in it failed to inform physicians and their patients about the risk of its mesh being cytotoxicity.

G. Ethicon's warnings and disclosures of adverse events in its TVT Instructions for Use ("IFU") are inadequate based on the adverse reactions and risks associated with the TVT that have been known to Ethicon from the time the TVT was first sold and marketed

The purpose of the IFU is for a medical device manufacturer to provide physicians with the information necessary for them to make decisions regarding the used a medical device for a particular patient. In addition, the IFU should disclose adverse reactions and risks known to the medical device manufacturer to the physician so that the risks can be relayed to the patient and an informed decision regarding the use of the product can be reached. Throughout my education, training, surgical and clinical practice, I have reviewed numerous IFUs for a variety of products, including mesh products in order to understand the proper way to use the device and to gain knowledge about the complications and adverse events associated with a device. I have extensive clinical experience with IFUs and instructing patients about the adverse events/risks contained in the IFU. Similar to Medical Directors, Dr. Martin Weisberg and Dr. David

Robinson, I have gained expertise in IFUs through my extensive clinical experience reviewing IFUs, and consenting patients regarding IFUs, including Ethicon's own pelvic mesh products including the TVT line and Prolift.

Catherine Beath, Ethicon's former Vice President of Quality Assurance and Regulatory Affairs, testified that "physicians should be made aware of all the significant safety risks associated with the product in the IFU."[199] And, "a reasonably prudent medical device company would continually update the label consistent with developing data and information that becomes known to the company" when it is appropriate.[200] Similarly, former Medical Director Dr. David Robinson testified that the warnings and adverse event section of the IFU should include all significant risks and complications related to the procedure and the mesh.[201] According to Dr. Robinson, a device manufacturer must include this information because you want to make sure the doctors have all the information they need to adequately inform patients who are deciding to use the product.[202] According to Ethicon Medical Director Dr. Martin Weisberg, the goal of the IFU is to communicate the most important safety risks attributable to the TVT device and that an IFU should never exclude known hazards or complications.[203] Dr. Weisberg also believes that an IFU should not knowingly underestimate the risks of using the product.[204] And, if an IFU excludes known complications or understates the risks, it "fails in one of its principal purposes."[205] Finally, Peter Cecchini, a 43 year Ethicon employee and Regulatory Fellow and the person responsible for the TVT 510K, testified that the "regulatory standard for the IFU is the known risks are supposed to be included in the adverse reactions."[206] Mr. Cecchini testified that he relies on medical affairs to

[199] Beath Dep. (7/12/13) 592:7-11.
[200] Beath Dep. (7/11/13) 198: 8-13.
[201] Robinson Dep. (9/11/13) 238:12-25.
[202] Robinson Dep. (9/11/13) 239:1-11.
[203] Weisberg Dep. (8/9/13) 659:19-660:15.
[204] *Id*. at 960:13-16.
[205] *Id*. at 961:10-17.
[206] Cecchini,10/22/12, 65:5-12.

make sure he knows the known risks so they can be included in the IFU.[207]

1. The TVT IFU Did Not Include All Known Risks, Was Inaccurate and Was Not Updated.

a. The IFU did not include all known risks.

As noted above, Ethicon did not include the proper information concerning the dissection in the original IFU. There were also numerous other potential risks that were not included in the IFU at launch.

If you compare the adverse reactions/risks in the TVT IFUs to the adverse reactions/risks that were available and known to Ethicon at the time of the launch of TVT, it is clear that there are numerous adverse events absent from the IFU. From the time TVT was launched in the United States in December of 1998 to the present day, there have been ten versions of the Ethicon TVT IFU. These include the following versions: October, 1998, April, 1999, May 1999, September 8, 2000, December 22, 2003, February 11, 2005, April 7, 2006, October 13, 2008, November 29, 2010, and May, 2015 A chart showing the Adverse Reactions/Risks section for each version of the TVT Instructions for Use is set forth below.

[207] Cecchini, 10/22/12, 65:18-24.

Product	Production Prefix	Start Bates	End Bates	First Use Date	Last Use Date	Adverse Reactions / Risks
TVT	ETH.MESH	00203477	00203482	10/27/98 (U.S Launch IFU)	04/11/99	*Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation and inflammation *As with all foreign bodies, PROLENE mesh may potentiate and existing infection. The Plastic sheath initially covering the PROLENE mesh is designed to minimize the risk of contamination *Over correction i.e. too much tension applied to the tape, may cause temporary or permanent lower urinary tract obstruction
TVT	ETH.MESH	00204514	00204519	04/11/99	05/18/99	Same as 10/27/1998 IFU

TVT	ETH.MESH	00204562	00204593	05/18/99	09/08/00	* Punctures or lacerations of vessels, nerves, bladder or bowel may occur during needle passage and may require surgical repair. * Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation and inflammation. * As with all foreign bodies, PROLENE Mesh may potentiate an existing infection. The plastic sheath initially covering the PROLENE Mesh is designed to minimize the risk of contamination. * Over correction, i.e., too much tension applied to the tape may cause temporary or permanent lower urinary tract obstruction.
TVT	ETH.MESH.	5225354	5225385	09/08/00	11/26/03	Same as 05/18/1999 IFU
TVT	ETH.MESH.	2340306	2340369	12/22/03	02/11/05	Same as 05/18/1999 IFU

TVT	ETH.MESH.	2340471	2340503	02/11/05	04/07/06	Same as 05/18/1999 IFU
TVT	ETH.MESH.	5222673	5222704	4/07/06	10/07/08	Same as 05/18/1999 IFU
TVT	ETH.MESH.	2340504	2340567	10/13/08	11/22/10	Same as 05/18/1999 IFU
TVT	ETH.MESH.	3427878	3427945	11/29/10	May, 2015	Same as 05/18/1999 IFU.
TVT	N/A	N/A	N/A	May, 2015	To Present Day	*Punctures or lacerations of vessels, nerves, structures or organs, including the bladder, urethra, or bowel, may occur and may require surgical repair. *Transitory local irritation at the wound site may occur. *As with any implant, a foreign body response may occur. This response could result in

						extrusion, erosion, exposure, fistula formation and/or inflammation. *Mesh extrusion, exposure, or erosion into the vagina or other structures or organs. *As with all surgical procedures, there is a risk of infection. As with all foreign bodies, PROLENE mesh may potentiate an existing infection. *Over correction, i.e., too much tension applied to the tape may cause temporary or permanent lower urinary tract obstruction. *Acute and/or chronic pain. *Voiding dysfunction. *Pain with intercourse which in some patients may not resolve. *Neuromuscular problems, including acute and/or chronic pain the groin, thigh, leg, pelvic and/or abdominal area may occur. *Recurrence of incontinence. *Bleeding including hemorrhage, or hematoma. *One or more revision surgeries may be necessary to treat these adverse reactions. *PROLENE mesh is a permanent implant that integrates into tissue, In cases in which the PROLENE mesh needs to be removed in part or whole, significant dissection may be required. *Seroma *Urge incontinence *Urinary frequency

						*Urinary Retention *Adhesion formation *Atypical vaginal discharge *Exposed mesh may cause pain or discomfort to the patient's partner during intercourse. *Death

In all six versions of the TVT IFU from May 19, 1999 to May of 2015, the Adverse Reactions/Risks section has remained exactly the same. It reads as follows:

> ADVERSE REACTIONS
>
> * Punctures or lacerations of vessels, nerves, bladder or bowel may occur during needle passage and may require surgical repair.
> * Transitory local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation and inflammation.
> * As with all foreign bodies, PROLENE Mesh may potentiate an existing infection. The plastic sheath initially covering the PROLENE Mesh is designed to minimize the risk of contamination.
> * Over correction, i.e., too much tension applied to the tape may cause temporary or permanent lower urinary tract obstruction.[208]

Despite only listing the above adverse reactions/risks, it is clear from the testimony of Senior Ethicon Employees in both the Medical Affairs and Regulatory Affairs that every adverse reaction/risk that Ethicon has scientific knowledge of today, it had scientific knowledge about at the time the TVT was first sold in and certainly in 2004 when the first TVT was sold, marketed and launched. Medical Director, Piet Hinoul testified that Ethicon understood the following adverse events occurred from the time the TVT was first sold, years before the first TVT was sold:

[208] ETH.MESH.02340406.

Erosions through vaginal epithelium Infection
Pain
Urinary Problems
Erosions that could decrease patient's quality of life
Dyspareunia
Need for additional surgeries
Need for the removal of device
Urinary Tract Infections
Dysuria
DeNovo Urgency
Mesh Exposure
Fistula Formation
Hematoma
Abscess Formation
Narrowing of vaginal wall
Erosion which can occur any time in future
Contracture of mesh causing pain
Complications making it impossible to have sexual relations
Worsening Incontinence

Yet, none of these were in the TVT IFU at launch. There have been two significant updates to the Adverse events section of the TVT IFU since launch, one in May of 1999, and one in May of 2015. The May, 1999 updates to the IFU, including the addition to the Adverse Reactions section, were part of a corrective action plan taken by Ethicon due to a number of Serious Adverse Events being reported with the TVT device, 25 of which came to light in the two months prior to the IFU update. The majority of these Adverse events involved injury to vessels, bladder or bowel.[209] The Adverse Events section of the IFU was updated in May of 1999 to include the following:

- **Punctures of lacerations of vessels, nerves, bladder, or bowel may occur during needle passage and may require surgical repair.**

In addition to the updates to the Adverse Reactions section of the IFU, the Warnings and precautions section was updated to include the following statements:

[209] ETH.MESH.07424335.

- The TVT procedure should be performed with care to avoid large vessels, nerves, bladder and bowel. Attention to local anatomy and proper passage of needles will minimize risks.
- Retropubic bleeding may occur postoperatively. Observe for symptoms or signs before releasing patient from hospital.

The May, 2015 IFU included a large number of significant updates, including warnings about pain, chronic pain, dyspareunia for the patient and/or her partner, need for multiple surgeries, and the difficulty in removing all or part of the device. These adverse events, which were added to the TVT IFU in May of 1999 and May of 2015, are all risks that Ethicon knew of at the time of launch of the TVT, and should have been included in the IFU since launch.

In addition, as discussed more fully throughout this report, Ethicon failed to include significant risks in its IFU related to the Prolene polypropylene mesh, including potential cytotoxicity, association with tumor formations and that the mesh can degrade, shrink and contract. The IFU also fails to include risks associated with the Prolene mesh, including chronic foreign body reaction, fibrotic bridging, infections/biofilms, fraying/particle loss and roping/curling of the mechanically cut mesh. Ethicon also failed to include that the laser cut mesh is three times stiffer than the mechanically cut mesh and that there are significant risks of erosions, pain, dyspareunia and urinary dysfunction associated with stiff, rigid meshes in the TVT-O manufactured with the laser cut mesh.

Moreover, the IFU fails to inform physicians that patients may require multiple surgeries to treat erosions, that erosions could be severe and untreatable, that patients could endure lifelong severe pain or dyspareunia/painful sex, removing the mesh and revision surgeries can be complicated and challenging for both the patient and physician, and complete removal of the TVT mesh is likely impossible.

Medical Director Dr. Weisberg testified that Ethicon did not include: “permanent,

lifelong, worsening and debilitating pain", lifelong risk of surgical repairs for erosions, "severe or chronic inflammation", collapse under strain and cause fibrotic bridging, that the product can degrade, that polypropylene is cytotoxic, severe erosion, or particle loss.[210]

But Ethicon did not disclose this information to physicians in its IFUs regarding characteristics of the old construction mesh in TVT, including that it is small pore, heavy weight mesh, it degrades over time, causes chronic foreign body reactions, fibrotic bridging, mesh contracture/shrinkage, fraying, particle loss, roping and curling of the mesh, and that it deforms and the pores collapse with tension. In fact, Ethicon medical director Piet Hinoul testified if Ethicon did warn that roping, curling and particle loss can cause pain and erosions Ethicon would have to take the mesh off the market.[211]

Moreover, the IFU failed to inform physicians of the frequency, duration and severity of the risks associated with the TVT device until the May, 2015 IFU update. In addition, former Medical Director, Dr. David Robinson, testified that Ethicon never informed physicians that patients may require multiple surgeries to treat erosions, that erosions could be severe and untreatable, and that patients could endure lifelong severe pain or dyspareunia/painful sex. This is true despite, as discussed above, Ethicon had scientific knowledge of the risks at the time of launch.

b. The IFU inaccurately portrayed risks.

In addition to excluding certain known risks, Ethicon significantly downplayed the risks that it actually listed in its IFU. This is especially true with respect to erosions. On the topic of erosions, in the Adverse Event/Risks section in the TVT IFU, in place from the time of launch until present day, it states:

Transitory local irritation at the wound site and a transitory foreign body

[210] Weisberg Dep. (8/9/13) 968:12-972:21.
[211] Trial testimony of Piet Hinoul, Batiste v. Ethicon, page 67.

> response may occur. This response could result in extrusion, erosion, fistula formation and inflammation.

This language significantly downplays the permanent nature of erosions and suggests to physicians that erosions are a "transitory" or temporary problem. As shown in an email exchange between Ethicon's Associate Medical Director of Worldwide Customer Quality Meng Chen, M.D., Ph.D and Bryan Lisa in the Regulatory Affairs Department, it was clear that the adverse events were not "transitory." Chen wrote, "Pardon me again, from what I see each day, these patient experiences are not "transitory" at all."[212]

Ethicon also had scientific evidence that erosions could occur many years after implantation of the device. In Minutes from June 22, 2001 Scientific Advisory Committee on Pelvic Floor Repair, it was a "Consensus: Erosion is a risk. Erosion, possibly an infection response. Typically seen by 3 mos, usually by 6-12 mos. Can present late, 3 years. To vagina- not a good situation. To bladder, urethra or rectum-a very bad situation."[213] "There have been reports of erosions into the urethra that are not picked up until months even years after the procedure."[214] In October 2002, Medical Director Dr. Martin Weisberg was involved in email exchange with European Science Director Axel Arnaud about downplaying risks with respect to erosions. Specifically, Dr. Arnaud suggested to Dr. Weisberg that Ethicon needed "to be more elusive" when discussing potential complications like erosions.[215]

According to Medical Director Dr. Martin Weisberg and former Medical Director Dr. David Robinson, Ethicon never disclosed or warned doctors or patients in IFUs or Patient Brochures that the use of TVT slings can cause lifelong risk of erosions.[216] Despite the fact Ethicon had scientific feedback from one of its own doctors that experiences were not

[212] ETH.MESH.04093125 (1/29/09 Email between Meng Chen and Bryan Lisa).
[213] ETH.MESH.02089392.
[214] ETH.MESH.04099233 (September 24, 2008 email fromMelissa Day to Meng Chen and others).
[215] ETH.MESH.03910175-03910177.
[216] Weisberg dep. (8/9/13) 968:2-969:10; Robinson Dep. (9/11/13) 329:12-330:7.

transitory and that she had concerns about the IFU and the transitory language, Ethicon never informed physicians or disclosed it in its IFU.

c. Ethicon failed to update the IFU.

Once TVT was on the market, Ethicon refused to appropriately update the IFU to reflect the known risks above and additional risks. On December 19, 2008, after Dr. Meng Chen had received a complaint from a number of patients about not being fully informed of the risks of the procedure, she recommended to senior management that the IFU be updated:

> [The patient] was given the most accurate consent for the potential adverse reaction known in 2005. However, we are in 2008 now, and there are two more TVT family products (TVTO and TVTS) on the market. Our post-market knowledge with these products are much more than what we have in the IFUs of all three types of TVTs (TVT-Abdominal, Obturator and Secur). My reason for bringing this point to you is maybe you may look into it from senior management perspective and to facilitate the IFU update for all three TVTs, particularly in the area of 'Potential Adverse Reactions'…. One of the paths for a better pre- operative consent is to provide an updated IFU to the operating physicians that reflecting the current knowledge of the manufacturer's on the potential adverse reactions."[217]

In a January 29, 2009 email, Meng Chen wrote again that the IFU should be updated to make it clear that the irritation and foreign body response were a result of the tape itself and that this "could result in tape extrusion, tape erosion, fistula formation or inflammation."[218] When working on the Mini-O/Abbrevo IFU, Ethicon employees noted that the older IFU's should be updated. Dr. Aaron Kirkemo wrote:

> I would agree from the meeting today that now that we have 12+ years of experience with TVT classic that learnings from the field would probably drive a relook at the TVT Classic IFU as reflected by some of your comments in this document."[219]

In response, Dr. Robison asked: "has there been agreement re: a project to revise TVT and

[217] ETH.MESH.04092868.
[218] ETH.MESH.04094863 (e-mail from Dr. Meng Chen to Bryan Lisa, Jan. 29, 2009).
[219] ETH.MESH.01239065 at 9066 (July 14, 2009 email from Aaron Kirkemo MD to Piet Hinoul MD and David Robinson MD).

TVTO?"[220] There was indeed agreement at upper management – there would be no revision to incorporate what they had learned: "Per Scott C and Stale, they just want to "look forward" with this project. Their plans are to leave TVT Classic [and TVT] as is. Aaron."[221]

Interestingly, in 2008, 2011, 2012, and 2015 Ethicon added numerous adverse reactions and risks to its Patient Brochures that have never been disclosed in previous versions of the Patient Brochures. Some of these adverse reactions and risk have never been disclosed in the TVT IFUs even at present time, and all of these were not in TVT IFUs prior to May, 2015 These risks are as follows:

From Patient Brochures (never in IFU prior to May, 2015. Those in Yellow are still not in IFU)
2008
Difficulty urinating Pain
Scarring
Mesh Exposure requiring treatment
2011
Mesh exposure into the vaginal canal
Mesh exposure associated with pain during intercourse for the patient and partner
Mesh exposure which may require removal of exposed mesh in office or operating room
2012
Pelvic Pain
Development of Urinary Incontinence
Voiding Difficulties
Hemorrhage or hematoma
Urinary tract infection Wound healing problems Injury to ureters
Pelvic abscess formation
Risk of infection
Vaginal scarring
Mesh contracture (mesh shortening due to scar tissue)
2015
Anesthesia risks
Pain (temporary or chronic)
Seroma
Neuro-muscular problems (including pain in the groin, thigh, leg, pelvic or abdominal area
Adhesion formation

[220] *Id.*
[221] *Id.*

> Abnormal vaginal discharge
> Recurrent incontinence
> Death
> These complications may require additional medical treatment, hospitalization, or surgery
> These complications may resolve over time or may be chronic
> There is also a risk that the mesh material may erode into another organ such as the bladder or urethra (mesh erosion) and cause pain and additional problems. Mesh erosion would likely require additional surgery to remove the mesh from the organ.

Some of these risks have been disclosed in Ethicon's other PROLENE mesh IFUs. For example, Ethicon's IFU for PROLENE hernia mesh states as follows: "The use of PROLENE Mesh in contaminated wounds should be with the understanding that subsequent infection may require removal of the material."[222] Even though Ethicon changed its Patient Brochures in 2011 and 2012 to include additional significant adverse events/risks, it never added the same information to the TVT IFU until May of 2015. This is true despite the fact that Ethicon had internal discussions about updating the IFU in 2009 after the 2008 FDA Public Health Notification (PHN). Specifically, a meeting was held to decide, among other issues, whether to update "the current Adverse Reaction of tape exposure and post-operative dyspareunia in the TVT-family products…."[223]

After discussing the 2008 PHN, competitors' labels and Remetrex issues, impressions were that tape exposure/erosion/extrusion were very frequently reported, patients did not feel there were adequate pre-op consent or risk-benefit assessment, patient specific concerns about exposure/erosion/extrusion, incontinence recurrence, post-operative dyspareunia and pain-affect quality of live and affect daily routine, re-operations and post-operative complications disproportionate to pre-operative-consent-expectations.[224] Despite these discussions and Ethicon's scientific knowledge of these serious, devastating and life-changing adverse

[222] ETH.MESH.02342102.
[223] ETH.MESH 04081189.
[224] *Id.*

events/risks, to this day, it has never updated or changed its IFU to include this information.

Repeatedly, the reason given for not updating an IFU to make it more accurate and safer was that doing so would threaten the launch timing of a new product. For example, when discussing the IFU for TVT-Exact, Dr. David Robinson cautioned against making too many changes from the original TVT-R IFU: "Just to clarify… the more changes we make to the IFU that differ from TVT-Classic, the higher the risk will be to the submission timing."[225]

In summary, Ethicon did not fully inform physicians about numerous adverse reactions/risks associated with the TVT despite the fact that Ethicon had scientific knowledge of the risks from the time the product was first sold. As a result, physicians were unable to fully consent and inform patients of the risk associated with TVT. In addition, some risks included by Ethicon in the IFU are mischaracterized to minimize the actual risk. Finally, when given numerous opportunities to update the IFU, and in the face of specific requests to do so from numerous medical professionals, Ethicon did not make the necessary updates. To a reasonable degree of medical certainty, this prevented physicians and patients the ability to make an informed choice regarding the use of the TVT. For a surgeon to properly inform the patient of all the known risks involved in any procedure involving an implantable medical device, the surgeon relies upon the manufacturer to have scientific knowledge of and convey all characteristics of its products that could impact safety and efficacy. Specifically, surgeons rely on the "Adverse Events/Risks" section of a medical device IFU to gain scientific knowledge regarding adverse events or undesirable effects that the company knows are associated with the product.

[225] ETH.MESH.10632650 at 10632652.

D. The TVT Device Is Not Designed for Special Patient Populations Nor Does the IFU or Marketing Inform Physicians or These Patients of Poorer Outcomes or Higher Risks.

Ethicon promoted the TVT as a "reproducible" technique that was appropriate for all patients. For example, Ethicon instructed its sales force to specifically target physicians to use the TVT and TVT in obese patients.[226] However, as Ethicon's Medical Director, Dr. Kirkemo, testified obese patients do not fare well with these devices.

> Q. One of the things that was actually shown in the TVT World study that you worked on was that for obese patients, for example, the efficacy was significantly down when slings were used in obese patients; is that correct?
> A. Obese people tend -- not to do as well.

In fact, Ethicon's study showed obese patients had about one half the success of those patients who were not obese. In addition, as Dr. Kirkemo testified, obese women suffered from more complications: "Their chance of success goes down. Their risk of complications goes up."[227]

Yet, Ethicon did not put this critical information into the IFU. Dr. Kirkemo testified:

> Q. Did you ever put that in the IFU?
> A. No….[228]

Not only did Ethicon not put this critical information in the IFU, Ethicon also did not inform patients:

> Q. Did you ever tell patients that in a single patient brochure, that if they were obese, their chances of this being successful were less than half?
> A. We did not.[229]

Ethicon also did not include information in its IFU about how the TVT had less efficacy and higher risk for older women or younger, active women.

> Q. Did you -- you also learned in the TVT World study, or maybe you knew this before, too, that being elderly decreased, or being very young, in fact, decreased the efficacy of the Ethicon sling procedures; correct?

[226] See, e.g., ETH.MESH.00640394 (trying to convince physicians to use TVT on obese patients); ETH.MESH.05119622 at 9623 (TVT "is a good choice for the obese patient or elderly patient….").
[227] Kirkemo Dep. (1/7/2014) 556:24-557:1.
[228] Kirkemo Dep. (1/7/2014) 556:4-19.
[229] Kirkemo Dep. (1/7/2014) 557:5-557:9.

A. With any incontinence operation, old people tend not to, you know, do as well.
Q. And was that ever put in a patient brochure or communicated to patients as far as you know?
A. As near as I can tell, in any marketing document, no.
Q. And what about the very young or the younger women; that was shown in TVT World that even younger women had lower efficacy; correct?
A. Some women that are very, very active can -- and have ISD can overcome the effect of the sling.
Q. In other words, the sling can fail.
A. The sling can be less than a hundred percent effective.
Q. And that was never actually communicated to patients as far as you know, correct, by Ethicon?
A: To my knowledge, no.
Q. And neither the older women or the younger women in issue we were just talking about, neither of those are included in the IFU; correct?
A: Those specific things are not mentioned.[230]

Ethicon also did not inform physicians and patients that the TVT devices, including the TVT would not work as well and would be more dangerous for women who smoked or who had Diabetes – a very large percentage of the patients to whom TVT was being marketed:

Q. Smoking decreases the efficacy of slings; correct?
A. Yes.
Q. Diabetes decreases the efficacy of slings; correct?
A. It can because you have neurologic, you know, disease.
Q. Neither smoking nor diabetes is listed as a potential contraindication or something special to look for in the IFU; correct?
A. It is not listed in the IFU….
Q. And Ethicon never communicated to patients that smoking would increase their risk of adverse outcomes or decrease the chance that the sling would work; correct?
A. We did not.
Q. And the same with diabetes. Ethicon never communicated to patients when they were selling TVT devices that diabetes would decrease the chance that the device would work or increase the chance that they would have an adverse event; correct?
A. I did not see that, no.

Ethicon knew that there were other patient populations that also faced increased risk or lower success rates with the TVT. Specifically, Ethicon knew that women who had prior pelvic surgery, prior pelvic injury or an infection, could be at increased risk if undergoing the

[230] Kirkemo Dep. (1/7/2014) 557:10-558:21.

TVT surgery. In 1999, Ethicon discussed putting another warning in the TVT IFU related to patients who had previous surgeries because of scar tissue.[231] The proposed warning was "patients who have had previous surgical procedures may require special consideration due to scar tissue."[232] Ethicon was concerned that the risk of mesh extrusion was increased in women with postoperative infection, previous vaginal surgery, vaginal atrophy or vaginal injury.[233] Dr. Isenberg, Ethicon medical director, admitted that if Ethicon knew this, it would have been reasonable to include a warning and, further, physicians and their patients would want to know this information. However, Ethicon was "under extreme pressure" to finish the IFU to meet a scheduled launch date in 1999, so did not include the statement in the April, 1999 IFU update.[234] Ethicon planned to discuss the issue for possible inclusion in the IFU in the future, but I have seen no evidence of such discussion, and this warning never made it into the IFU. Again, despite these discussions in 1999 and former Medical Director Dr. Isenberg's opinions that it would be reasonable to have this information in the IFU, to this day, this critical information remains absent from the IFU.

Finally, Ethicon also knew that the method of anesthesia utilized during the TVT surgery could affect patients' outcomes, but didn't disclose that information to physicians or patients. Ethicon's internal documents, including interviews with Ethicon's key opinion leader, Dr. Carl Nilsson, Ethicon U.S. Marketing Research documents, and letters from the inventor of the TVT (Dr. Ulmsten) show that Ethicon knew that performing the TVT procedure under general anesthesia as opposed to local anesthesia decreased the chance for success of the surgery and also increased a patient's risk of urinary retention and erosions.[235] This is further supported by the testimony of Dr. Richard Isenberg, a former medical director for Ethicon, who was at

[231] ETH.MESH.08505071, ETH.MESH.00203456, Eth.Mesh.00159634-00159719 at 00159697.
[232] ETH.MESH.08505291.
[233] *Id.*
[234] ETH.MESH.00203456.
[235] Eth.Mesh.04048515-04048520; Eth.Mesh.00130934-00130941, Eth.Mesh. 00400954-00400956.

Ethicon just after the initial launch of the TVT.[236] Dr. Isenberg testified that the IFU could be better worded so that physicians knew that local anesthesia should be preferred over general anesthesia.[237] In addition, according to Dr. Isenberg, Dr. Ulmsten, inventor of the product, informed Ethicon that the TVT procedure should be carried out under local anesthesia unless it was a special situation.[238] Despite the inventor's desire to have this language listed, to this day, it does not appear in the IFU.[239] Dr. Isenberg was also aware that using general anesthesia could cause the success rate of the procedure to go down and put the patient at increased risk for urinary retention and erosions.[240] He testified that he believes a responsible company should have put this information in the IFU because the IFU is the one document that you can count on every physician receiving.[241] I agree. Again, however, to this day, this warning does not appear in the TVT IFU.

The TVT is dangerous and can cause significant, lifelong injury to women, due in part to its "one-size fits all" design. Ethicon failed to inform physicians that there are certain patient populations that face greater risks and less success with the TVT. Ethicon needed to pass this critical information on to physicians in the IFU so that they could have an appropriate informed consent discussion with their patients.

Accordingly, it is my opinion to a reasonable degree of medical certainty that the TVT as designed is not effective for special patient populations. In addition, the TVT is dangerous and can cause significant, lifelong injury due in part to its "one-size fits all" design. Moreover, Ethicon failed to inform physicians of the importance of these patient variations and the potential for permanent, serious injury from the TVT. Because Ethicon failed to inform

[236] Isenberg, 11/6/13, 461:16-530:13.
[237] Id. at 526:25-528-18.
[238] Id. at 553:15-554:21.
[239] *Id.*
[240] Id. at 566:9-15.
[241] Id. at 566:3-8.

physicians, Ethicon also removed the ability of the physicians to fully inform patients of these risks.

E. Ethicon failed to reveal material facts about complications and conflict of interests regarding data promoted in the materials.

Since the TVT was first launched, Ethicon has sent materials in various forms to physicians promoting long term follow up data on the original cohort of patients implanted with the TVT from 1995-1996.[242] Ethicon continued to cite to this data in its TVT materials.[243] In addition, the materials tout low complication rates related to various adverse reactions, including erosions. These materials include press releases, marketing brochures and email blasts.

The long term data primarily relied on by Ethicon throughout these materials relates to the Ulmsten/Nillson studies. These studies were originally started by Dr. Ulmsten, the inventor of the TVT, and continued by Dr. Nillson after Dr. Ulmsten's death. Prior to selling the TVT to Johnson & Johnson, Dr. Ulmsten owned a company called Medscand. As discussed more fully below, Johnson & Johnson hired Dr. Ulmsten and Medscand to conduct studies related to the TVT. To this day, Ethicon relies heavily on these studies and uses them in numerous promotional materials despite the fact that Ethicon never disclosed to physicians the potential conflict of interest and inherent bias that exists due to Dr. Ulmsten's relationship with Ethicon and Johnson & Johnson. In addition, Ethicon never disclosed to physicians that the device used in the original Medscand study was different than the TVT device. It is important to physicians using the TVT that the data in these types of promotional materials is accurate, unbiased and that physicians are informed about any potential conflicts of interest in the data contained within the materials. In other words, physicians rely on Ethicon to provide fair and balanced

[242] ETH.MESH.0015598, ETH.MESH.00658058, ETH.MESH.01186068, ETH.MESH.02236784, ETH.MESH.02237103, ETH.MESH.03459211, ETH.MESH.05183409, ETH.MESH.00339437; ETH.MESH.05794787.
[243] ETH.MESH.00163582.

information and to ensure that physician have been given all the data and not just the positive press release data.

Despite using the Ulmsten data to promote the TVT, Ethicon never disclosed to physicians the bias and inherent conflict of interest related to the Ulmsten data. Specifically, in its promotional materials, Ethicon (Johnson and Johnson) never informed physicians about its relationship and contracts with Professor Ulmsten and his company Medscand. It is clear from the contracts that the publications and data from Dr. Ulmsten where contracted for hire by Johnson and Johnson International.[244]

The License and Supply Agreement between Johnson and Johnson International and Medscand (Ulmsten's Company) dated February 13, 1997, states in section 3.6 Milestone Payments:

> Johnson and Johnson International (JJI) shall pay shall pay to Medscand the following payments (b). A payment in the amount of $400,000.00 due on February 28, 1997; provided, however, that in the event that Clinical Trials as specified in Exhibit C have not been completed by such date, then such amount shall not be due until the completion of the Clinical Trials.[245]

Under Exhibit F, Consulting Agreement with Professor Alf Ivar Ulmsten, section 4 Confidential Information Rights to Inventions and Copyrights (B) it states:

> Any copyrightable work whether published or unpublished created by supplier Dr. Ulmsten directly as a result of or during the performance of services herein shall be considered a work made for hire, to the fullest extent permitted by law and all rights, titles and interest herein, including worldwide copyrights shall be the property of the company as the employer and party specially commissioned said work.[246]

Finally, in Exhibit C, Clinical Trials, it states:

> The results of clinical trials will be considered acceptable if, first, they do not differ significantly from the results published in the original article published in the Int. Urogynecol J 1996-7:81-86 by U. Ulmsten, et.al., with regards to the

[244] ETH.MESH.08696085 at 085-6134.
[245] ETH.MESH.08696091.
[246] ETH.MESH.0869116.

> following items: Safety 1.1, preoperative complications 1.2 , post operative complications 1 year from operation 2. Efficacy. Second Long term results over 1 year from operation do not show a deterioration of rates significantly different from those of the standard suburethral slingplasties. It is assumed that from 12 – 60 months a gradual decrease in efficacy of 5% is normal. 3. No significant numbers of unexpected i.e. not addressed in the original article published in the Int. Urogynecol J 19967 81-86 by U.Ulmsten at et.al. procedure related i.e. not addressed in the review article published in the Int. Urogynecol J 19945: 228-239 by G. N. Ghomiem et.al. complications appear at any time in the postoperative course.[247]

In total, Dr. Ulmsten stood to gain millions of dollars for the 6 papers that he published on the TVT device. In addition, the results of those studies would be found acceptable for payment only if they did not differ from the parameters sent by Johnson & Johnson regarding complications and efficacy. The Ulmsten studies have an inherent conflict of interest and bias as they were "made for hire" and standards were set by Johnson & Johnson. As set forth above, if Dr. Ulmsten did not meet the standards set forth by Johnson & Johnson, he did not receive substantial payments for the "studies." As a result of this relationship, there is a clear conflict of interest and potential for enormous bias issues.

The conflict of interest and bias created by the relationship between Ethicon and Dr. Ulmsten was acknowledged by Dr. Axel Arnaud, Ethicon's European Medical Director, in a recent deposition. Specifically, Dr. Arnaud testified that such an agreement like the one discussed above between Dr. Ulmsten and Johnson & Johnson creates a potential conflict of interest.[248] Dr. Arnaud also acknowledged that when Johnson & Johnson enters into this type of agreement with a physician or his company and the study is published, there "certainly" needs to be a disclosure of the relationship.[249] Additionally, Former Ethicon Medical Director, Dr. David Robinson, testified that in his experience working in the industry for medical device

[247] ETH.MESH.08696132.
[248] Arnaud Dep. (7/20/13) 497:24-501:21, 509:8-17.
[249] Arnaud Dep. (7/20/13) 514:17-515:1.

manufacturers, it is best that potential biases be disclosed.[250] He also testified that if publications from somebody like Ulmsten or Nilsson about safety and efficacy are being published, it is best if they disclose that they have a financial bias or conflict of interest.[251] In fact, in an April 2009 email exchange with Medical Director Piet Hinoul about a physician who, like Ulmsten, is a consultant and inventor for competitor Boston Scientific, Dr. Robinson states that that situation presents "enormous bias issues."[252] Despite two of its medical directors testifying that the relationship between Ulmsten and carried over to Nilsson presents a conflict of interest and bias, Ethicon has never disclosed this information in its promotional pieces. This is information physicians and patients have a right to know so that a proper informed decision regarding the value of the data in the studies and the use of the product can be made.

Aside from never disclosing to physicians the underlying conflict of interest and bias of the Ulmsten studies in its promotional pieces, Ethicon also never informed them about other problems with the data, including incomplete data on the original cohort, data incorrectly reported and erosion rates underreported. In the original 510k submission for TVT Classic, Ethicon used Medscand data from the Scandinavian Multicenter Study.[253] The report shows that 12 month follow was obtained for 90 of the original 131 patients, without explanation of why there was a loss of 41 patients from the study. The study also describes a complication of wound infection: "while the vaginal infection required surgical intervention with resection of exposed mesh." This represents a vaginal mesh erosion/extrusion/ exposure and needs to be reported as such. However, when the paper was published (Ulmsten, Int Urogynecol J 1998), the paper states that there was no defect healing and no tape rejections. It further misrepresents

[250] Robinson Dep. (9/11/13) 214:15-21.
[251] Robinson Dep. (9/11/12) 215:8-13.
[252] ETH.MESH.03259439; Robinson Dep. (9/11/13) 219:6-220:10.
[253] ETH.MESH 00371587.

the outcome for this patient as "The patient with the wound infection had vaginal atrophy. After minimal vaginal wall resection and effective local estrogen treatment she healed without further intervention. There was no tape rejection."

If Ulmsten had reported a mesh erosion/extrusion/exposure with mesh excision in his study, it would not have been acceptable under Exhibit C of his consulting contract for payment of the $400,000.[254] This demonstrates that the results of this paper were potentially biased by the payment Ulmsten would receive for favorable data and should discount the data. At the very least, Ethicon should have informed physicians about the relationship between Ethicon and the Ulmsten studies.

Many of the marketing brochures tout the "[t]he urethral erosion rate less than or equal to that of traditional slings; no reported urethral erosions in 10 studies of 50+ patients."[255] The reference used for the first part of this statement is from Dr. Gary Leach) who looked at traditional sling procedures done before 1993, when traditional slings were performed at the bladder neck and purposely placed under tension to treat severe stress urinary incontinence from intrinsic sphincter deficiency (particularly among Urogynecologists).

The second part of this statement regarding "no uretheral erosions" is incorrect. In published studies, Dr. Karram found one case of urethral erosion in his study of 350 Gynecare TVTs performed (Karram Obstet Gynecol 2003) and Hammad found nine cases of urethral erosion in his study (Hammad Eur Urol 2005).[256] His study followed the complications of 1459 patients 993 of whom had Gynecare TVT, while the remainder has SPARC procedures. While the authors do not break down the incidence of urethral erosion by product, it is exceedingly unlikely that all erosions happen in the SPARC group.

[254] ETH.MESH 08696132.
[255] ETH.MESH 00339439.
[256] Karram, M.M., et al., *Complications and untoward effects of the tension-free vaginal tape procedure*, Ob & Gyn 2003, 101:929-32.

The statement regarding "no uretheral erosions" also did not include deTayrac's 2003 paper of 61 patients (31 TVTs) which showed a 3% urethral erosion rate.[257] Dr. Shlomo Raz described a study of 26 patients who presented with voiding dysfunction, including symptoms of severe urethral, pelvic and genital pain, urinary retention, recurrent UTIs, de-novo urgency with urge incontinence found to have mesh from a sling procedure in the bladder or urethra.[258] Their patients were found to have been treated conservatively with anticholinergic medication. They conclude that "dysfunctional voiding symptoms after sling procedure should elicit a high degree of suspicion if pharmacotherapy is not successful in alleviating symptoms...Cystoscopy should be considered if the patient remains symptomatic despite pharmacotherapy."

In one of the Nilsson studies, Dr. Nilsson describes four patients on "anticolinergics" (Int Urogynecol J 2008 Table 3). They conclude: "It is also encouraging to see that no late adverse effects of the polypropylene tape material was found and that erosion of the tape into adjacent tissue did not occur." However, this statement cannot be made for 4 patients who are on pharmacotherapy without a cystoscopy, which was not performed in the 11 year follow-up study. Dr. Raz's review of the literature found multiple cases of urethral erosions in a large series with TVT.[259] There have also been multiple case reports attesting to the fact that urethral erosion does occur specifically with Gynecare TVT products.[260] To imply that urethral erosion does not occur is not giving physicians fair and balanced information about the true incidence of urethral erosions with TVT products.

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[257] de Tayrac, R., et al, *A prospective randomized trial comparing tension-free vaginal tape for surgical treatment of stress urinary incontinence*, Am J Obstet Gynecol 2004, 190:602-8.
[258] Deng D.Y., et al., *Presentation and management of major complications of midurethral slings: Are complications under reported*, Neurourology Urodynamics 2007, 26:46-52.
[259] Karram 2003, Hammad 2005.
[260] Sweat, S., et al, *Polypropylene Mesh Tape for Stress Urinary Incontinence: Complication of Urethral Erosion and Outlet Obstruction*, J Urology 2002, 168:144-146; Gerstenbluth, R.E., et al, *Simultaneous Urethral Erosion of Tension-Free Vaginal Tape and Woven Polyester Pubovaginal Sling*, J Urol. 2003, (2 Pt 1) 170:525-6; Vassallo, B.J.., et al., *Management of latrogenic Vaginal Constriction*, Am J Obstet Gynecol 2003, 102(3):512-20; Haferkamp, A., et al., *Urethral Erosion of Tension-Free Vaginal Tape*, J Urol 2002, 167(1): 250.

Later, Nilsson publishes the 5 year follow-up of this cohort.[261] He describes the cohort: "a prospective open multicenter trial was conducted in the Nordic countries at the beginning of 1995. The short-term results were published in 1998." This implies that these are the same patients as published in 1998. It is interesting or an incredible coincidence that the exact number of patients receiving 12 months of follow-up in the Medscand publication (90) was the exact number being described in the 5 year study. There is again no mention of the outcome of the other 41 patients from the original cohort. Another interesting detail in the 5 year study is that the original number of centers used for the study (6) was now down to 3, again without explanation. The 5 year report does describe the original patient with the wound infection but again fails to mention she had mesh excised, "1 case (1.1%) of infection of operating site was observed."

In 2006, Dr. Nilsson published a different study on long term outcome of patients with TVT.[262] He describes his new patient population: "A multi-center study comprising only carefully selected primary cases revealed a promising cure rate of 85% after 5 years (reference his 5 year study) and 81% at 7 years."[263] These two papers are the subject of many press releases and marketing brochures, but they never described that these were carefully selected patients. "To our knowledge, the long-term effect and effectiveness of the TVT procedure has not yet been studied in an unselected patient group. We earlier reported 16-month follow-up results of a general patient group referred to a tertiary medical unit and comprising primary, recurrent, mixed, and low pressure urethra cases. In the present study, we report the long-term results in the same above-mentioned group." They describe a 3.1% mesh "visualized" rate, half of which needed surgical resection. These results, more representative of what one would see

[261] Ulmsten data; Nilsson, Int Urogynecol J 2001.
[262] Kuuva , N., et al., *Long-term results of the tension-free vaginal tape operation in an unselected group of 129 stress incontinent women*, Acta Obstetricia Gynecologica Scandanavica 2006, 85:4 482-87.
[263] Nilsson, Obstet Gynecol 2004.

in a normal practice, is never mentioned in press releases or marketing documents.

Conversely, when Ethicon receives adverse information, it does not make it into the promotional pieces. Dr. AC Wang's abstract, "Tension-Free Vaginal Tape (TVT) for Urinary Stress Incontinence - A Preliminary Report" was used in the original 510k submission in October of 1997 as support for FDA clearance of the TVT.[264] However, when Dr. Wang reported that he had 25 cases of "failure of vaginal healing considered by him to be potential tape rejection...in each case the revision failed within 2 weeks, requiring further surgery to excise mesh and repair the vaginal wound," this important information never made it into the marketing materials or press releases.[265]

The long-term follow-up data (Ulmsten/Nillson data) used by Ethicon to promote the lack of risk of TVT is spurious at best. We have incomplete data on the original cohort, data that is falsely reported, original sites that were excluded without explanation and a lead investigator who had a significant relationship and financial incentive to reach certain results with the data. This is the same data which is now used repeatedly in promotional and marketing materials sent to physicians.

K. The Benefits of the TVT are Outweighed by the Severe, Debilitating and Life Changing Complications Associated with TVT

It is my opinion, based on my training, experience and extensive review of the literature and Ethicon's internal documents that the benefits of the TVT are outweighed by the severe, debilitating and life changing complications associated with the medical device. It is clear that a substantial number of women who are implanted with the TVT have already and will continue to suffer chronic, debilitating erosions or pain, among other complications, and these life changing complications outweigh the benefits of the TVT, a device used to treat a quality

[264] ETH.MESH.00371551.
[265] ETH.MESH.00409675.

of life issue.

This is especially true given that traditional surgeries like the Burch and pubovaginal slings are not associated with the frequency or extent of these life changing complications. The efficacy of the TVT is equivalent to the traditional surgeries like the Burch. Traditional surgeries are not associated with TVT mesh based complications like contraction and erosion, however, with clinically significant erosion. And, further, although traditional surgeries can cause symptoms such as pain following surgery, including dyspareunia, the risk, duration, extent and severity of chronic pain including dyspareunia following the TVT is much greater than with traditional surgeries, and of course those surgeries do not result in the often untreatable complications and symptoms that result from the TVT mesh.

There were reasonably feasible safer alternatives available to Ethicon for the treatment of patients in this case. For example, the Burch procedure would have been an appropriate treatment for the stress urinary incontinence. The Burch procedure eliminates the risks specifically associated with the old construction heavyweight mesh used in the TVT because the Burch procedure does not require the use of mesh. Another feasible safer alternative to the TVT would have included autologous fascia slings. Sutures used in an alternative design to the TVT (i.e., Burch); an autologous fascial sling; or, an allograft sling (i.e., Repliform) would have been a safer alternative design to the TVT.

Moreover, because of the manufacturing defect present in the mechanical cut mesh and laser cut mesh, several additional feasible alternatives were available to Ethicon that would have been less dangerous. As I have testified in previous cases where women have suffered permanent debilitating injuries from TVT mesh products, these alternatives depend on the patient, patient's lifestyle, patient's medical history, and the injuries the patient suffers from. When patients are young and active at the time of surgery, and when the mesh

contains a manufacturing defect making the mechanical cut mesh especially prone to losing particles, fraying and deformation and because of injuries and risks from the TVT device, certain lighter weight, larger pore mesh resistant to fraying, deformation, shrinkage and particle loss both by design and by improved manufacturing, and include a less invasive implantation method than that used with the TVT would have been less dangerous and a feasible alternative. When the mesh contains a manufacturing defect making the laser cut mesh especially prone to stiffness and rigidity, and because of injuries and risks from the TVT device, certain lighter weight, larger pore mesh resistant to excessive stiffness and rigidity both by design and by improved manufacturing, and include a less invasive implantation method than that used with the TVT would have been less dangerous and a feasible alternative.

In addition, based on Ethicon's internal documents, deposition testimony, and the medical literature, feasible alternatives would have included individually or collectively a lighter weight, larger pore mesh material. Indeed, Ethicon had lighter weight larger pore meshes that were less stiff and more compliant with patients' tissues that Ethicon marketed for use in the pelvis. A midurethral sling device made from PVDF, (e.g., Dynamesh), or a mesh sling with less polypropylene and sealed edges, or a sling which contained a shorter piece of mesh and had arms consisting of suture like material would have also been a safer alternative.

Additionally, I continue to review internal Ethicon documents and the relevant body of medical literature on a continual basis. I also see women with chronic mesh complications on a continual basis. When I evaluate these women, whether it is in my practice or in a litigation setting, I see life-altering injuries that are related to the type of mesh these women were implanted with, the method in which the mesh was implanted,

where the mesh was implanted, but also the patient's lifestyle and makeup. In many of these cases, where one option may be less dangerous for a certain patient, in another patient that same option may be more dangerous. This is because of the unique patient specific concerns that pelvic floor surgeons, like myself, encounter on a daily basis when evaluating medical treatment for specific patients. Indeed, Ethicon and the inventor of the TVT recognized this very concept.

Unfortunately, although there have been a large number of studies and publications involving the TVT over the years, the quality of most of the studies is not good, and the amount of bias included in the studies and publications adds to the limited value that the studies offer about long term, severe and debilitating complications like chronic pain and erosions associated with the TVT. The most recent Cochrane review of mid-urethral slings, Ogah (2011), concluded that most trials involving mid-urethral slings had short follow-up and the quality of evidence was variable such that the quality of evidence for the majority of trials was moderate with a minority having low-to-moderate evidence.[266] Few trials reported outcomes after 1 year and long term adverse effects had yet to be determined. There are only a handful of RCTs involving the TVT that are long term, and major and long term complications would unlikely be picked up in these RCTs in part because they are designed with a primary endpoint of efficacy, not safety. The true incidence are more likely to be determined by registries or databases, but published registries do not track certain complications such as pain or dyspareunia, and have not been designed to monitor long term problems (Tamussino, 2001 and 2007; Kuuva 2002, Collinet, 2008, Dykorn 2010). This void in studying and presenting the true incidence and nature of long term and life altering complications, along with the biases inherent in many of the studies, and other factors, negates the value of the large majority of the

[266] Ohah, et. al., Minimally Invasive Synthetic Suburethral Sling Operations for Stress Unrinary Incontinence in Women: A Short Version Cochrane Review. Neurology and Urodynamics 30:284-291 (2011).

studies, and as a result, other sources of data such as published case series are relevant and important to truly understand the nature of these complications. Ethicon's internal documents and data, which are not publically available, present a very different picture of the TVT than the information that has been shared with patients and physicians.

I have done an in-depth review and analysis of the studies, and am prepared to discuss the studies including the small number of studies that have tracked chronic pain, dyspareunia and erosions on a long term basis. The Abbott study is particularly noteworthy, however. Abbott (2014) described a series of 347 patients evaluated for mesh related complications from 2006 -2010. Approximately 50% had a sling only and an additional 26% had a sling and TVM mesh. The median time from placement to evaluation was 5.8 months with a range of 0 – 65.2. This would mean that many of these patients would not have been captured in registries or RCT's with one year or less follow-up. Also only 26% were seen by another facility before attending one of the study sites, meaning that at least ¾ of these complications were not known to the implanting physician, again highlighting the limited utility of data at the primary site. The authors found 30% of patients had dyspareunia, 43% had erosion and 35% had pelvic pain.[267] This study highlights the degree and severity of the complications that mesh slings like the TVT are causing and, importantly, that physicians in the real world simply do not have the information about the severity of the problem. This is why it is extremely important for manufacturers of slings like Ethicon to accurately and fully report the risks and complications associated with the mesh devices to doctors – something Ethicon simply has not done.

L. It has been known since the launch of the TVT that the mesh can be difficult to remove, is susceptible to degradation, can rope, curl, deform, fray, and lose particles, and is a heavy weight mesh. However, Ethicon did not account for this facts in its dFMEA at the time of launch, and has failed to complete a proper risk analysis of these hazards

[267] Abbott, et. al., Evaluation and management of complications from synthetic mesh after pelvic reconstructive surgery: a multicenter study. American Journal of Obstetrics & Gynecology. (Feb. 2014).

Ethicon adopted revision 8 of the "Preventia" risk analysis prepared by Medscand AB for the TVT device as part of the TVT design history file.[268] This risk assessment was done on July 12, 2000, and omits numerous risks including that the mesh (1) can be difficult to remove, (2) is susceptible to degradation, (3) can rope, curl, deform (4) fray, and lose particles, and (5) is a heavy weight mesh. Ethicon does not have the previous versions of the risk assessments, revisions 1-7, which would include the version of the risk assessment performed prior to the launch of the TVT in late 1998, but it is reasonable to assume that if these risks had been identified in prior versions, they would still appear in revision 8 dated in July of 2000.[269] In April of 2002, Ethicon identified 11 risks that had been omitted from the Preventia revision 8 risk assessment. These risks include:

- Vaginal Extrusion
- Erosion/Urethral
- Perforation by Mesh
- Infection
- Vaginal Incision
- Urethral Tear
- Mesh Broken
- Torn Mesh
- Bent Needle
- Mesh Kinked(Twisted)
- Dull Needle

These are all risks that Ethicon knew or should have known at the time of launch of the TVT, and thus should have been assessed prior to launch. Because Ethicon failed to even identify these eleven risks, they also failed to assess the predicted and actual severity and frequency of these events, overall risk score, and actions needed to mitigate the risks of these failures. In addition, Ethicon also failed to identify and assess the other five risks discussed above at the time of launch 1998, or in 2002 when 11 new risks were identified, and still has

[268] ETH.MESH.01317508.
[269] Deposition of Dan Smith, 06-04-2013 794:8-18. Mr. Smith testified that "no person at Ethicon."

not conducted a proper risk analysis to this day.

Ethicon clearly did not consider and analyze that TVT mesh (1) can be difficult to remove, (2) is susceptible to degradation, (3) can rope, curl, deform (4) fray, and lose particles, and (5) is a heavy weight mesh as potential failure modes. These were critical analyses in designing and marketing the TVT product and needed to be performed to conduct an appropriate risk analysis and mitigation strategy. There is no mention of these failure modes in the dFMEA in Ethicon's possession at launch, and there has been no proper analysis of these failure modes to this day. It is opinion that Ethicon has failed to meet the standard of care of a reasonable device manufacturer by failing to include these known risks associated with the TVT device on its risk assessments at launch, and has failed to properly assess these known risks to this day.

V. CONCLUSION.

Ethicon has marketed and sold the TVT despite the fact that it is contains numerous characteristics that make it unsuitable for implantation in a woman's vagina. These characteristics include the following: (1) degradation of the mesh; (2) chronic foreign body reaction; (3) fraying, sharp edges and particle loss; (4) Infections and Bio-films; (5) roping and curling of the mesh; (6) loss of pore size with tension; (7) fibrotic bridging leading to scar plate formation and mesh encapsulation; and (8) shrinkage/contraction of the encapsulated mesh.

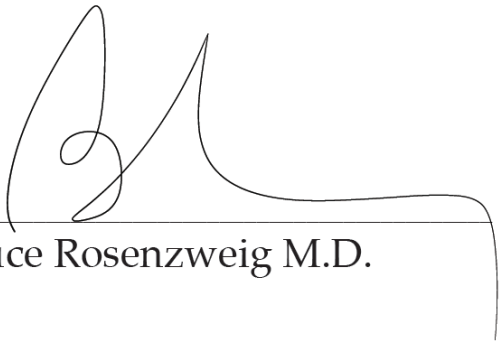
Not only does Ethicon sell a product which should never be put in the vagina, it failed to inform physicians and their patients about numerous risks associated with the product despite the fact that these risks were known before the product was launched. Ethicon has removed the ability of physicians to appropriately inform their patients of the risks and

benefits of the TVT and made it impossible for women to consent to the procedure. In addition, despite having knowledge to the contrary, Ethicon never informed physicians and their patients that the TVT could be toxic to their bodies. Finally, while keeping this information from women, Ethicon marketed its product with promotional pieces that did not disclose key conflict of interest information or the true complication rates of its products.

As a result of these failures as fully set forth in this report, the TVT has caused and will continue to cause a multitude of injuries in women, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, nerve injury, recurrence, worsening incontinence, chronic dyspareunia, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others.

All opinions I have are to a reasonable degree of medical certainty. I understand discovery is still ongoing in this case and I reserve my right to amend my opinions if further information is provided in any form including, but not limited to, corporate documents, depositions and expert reports of both Plaintiff and Defense experts. I have also reviewed the opinions of Dr. Uwe Klinge, Dr. Muhl, Dr. Vladimir Iakovlev, Dr. Elliott, and Dr. Anne Wilson, and incorporate those opinions herein. I also incorporate my past reports and testimony concerning the defects in the TVT and TVT-O.

Signed this 22nd day of May 2017.

X 

Bruce Rosenzweig M.D.